A CASE OF TUBERCULOUS MENINGITIS WITH SECONDARY INFECTION.

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Cases of tuberculous meningitis with secondary infection are sufficiently rare to justify the report of a single case.

The patient, L. F., male, white, 20 years of age, a drug clerk by occupation, was admitted to the service of Dr. John H. Musser at the University Hospital on March 15, 1902. His family history was negative; his previous history was also unimportant, with the exception of one or two attacks of gonorrhea (the last attack occurring within a year of his admission), and an eruption on the skin of the thighs and abdomen occurring shortly before his admission. Otherwise he had always been strong and healthy. His illness commenced with severe headache, nausea, vomiting and diarrhea, and he was obliged to stop work. He developed stiffness and soreness in the back and neck, and suffered from severe pain, starting in his eyes and radiating backward. He was treated for typhoid fever until March 8th, and with the exception of the pain in his head gradually improved. On the 12th of March he became delirious, and continued so until his admission to the hospital on March 15th. On the day after his admission the blood was tested, with the following results: Hemoglobin, 105 per cent; R. B. C., 5,870,000; W. B. C., 10,740 (2.30 P. M.). The urine was light amber, clear, acid and gave no precipitate. The specific gravity was 1030. There was no albumin and no sugar. The diazo reaction was negative. There was a trace of indican, and the chlorides were normal. Lumbar puncture was performed and yielded about 50 cc. of clear colorless fluid, containing a few small flakes of fibrin (?). This fluid responded to the copper test for pyrocatechin, and also showed a pronounced albumin reaction. Smears showed the presence of a diplococcus. The Widal reaction was negative. The patient continued delirious. The following notes were made the day after his admission..

"The patient is apathetic but entirely conscious, and responds intelligently when spoken to. The face is slightly flushed; the conjunctivæ are slightly injected; the left pupil is larger than the right. There is general hyperesthesia. The tongue is dry and covered with a yellowish brown coat; it is red at the edges. The respiration is chiefly abdominal. The abdomen is slightly retracted. The pulse is medium full, compressible, and the artery is distinctly sclerotic. The apex beat is in the fifth interspace in the nipple line; is powerful, appears to diffuse and descend during systole. The first sound is greatly accentuated, and the second sound is clear and sharp. There is a loud, short systolic murmur accompanying the first sound. At the base both second sounds are greatly accentuated, and the aortic second sound is louder than the pulmonic, but there are no murmurs. On the right side the respirations are loud and vesicular, and there are no râles. On the left side laterally there is an interrupted inspiration, consisting of a series of blowing sounds synchronous with the heart-beat. Stroking the skin causes a distinct, slowly developing tâche, spreading about a quarter of an inch to either side; and there is an erythematous eruption over the clavicles, chest and left shoulder. The spleen is not palpable. Kernig's sign is present on both sides; the knee jerks are absent; and there is no spasticity of the limbs. The pupils react sluggishly to light, but there is no apparent paralysis of the ocular muscles.

On the following day Kernig's sign was more pronounced than before. There was no Babinski phenomenon, and the knee-jerks and ankle clonus were still absent. The patient responded slowly to external stimulation, and there was spontaneous movement in both arms. The area of cardiac dulness commenced above at the fourth rib; on the right at the midsternum, and on the left at about half an inch inside the nipple line. The cardiac condition was practically the same as upon the previous examination. Both lungs were resonant anteriorly, and harsh, moist râles, a few on the right and several on the left side, were heard. The percussion resonance was somewhat impaired on the left side posteriorly. The patient was comatose and edema of the lungs had developed. The leucocytes were 17,400 at 9 A. M. On the 18th of March the patient was slightly improved, and the edema of the lungs had disappeared. Cyanosis, however, was marked, and he had incontinence of urine. The leucocytes were 17,000. His condition remained about the same until March 20th, when there was muttering delirium and twitchings in the hands, arms and face. The heart's action was regular but weak, the pulse small and rapid, there was increasing pulmonary edema, and the patient died about 3 P. M.

Lumbar puncture was performed twice. On the first occasion (March 16) about 30 cc. of fluid were obtained with the reactions already described. On the second occasion (March 17) about 10 cc. of fluid of the same character were withdrawn. On both occasions strict asepsis was observed, and the fluid collected in sterile test tubes. It was given to Dr. Kneass for bacteriological examination. The cultures were made upon agar, blood serum, gelatine, and in various other media, and on both occasions the same micro-organism was found. It corresponded in all cultural and morphological respects to the micrococcus tetragenous, and it was supposed, until the result of the autopsy was known, that we had to do with a meningitis produced by this micro-organism. Unfortunately, inoculations were not made with the fluid, but smears, stained for tubercle bacilli, were negative.

The autopsy was performed by Dr. Hendrickson, who made the following informal report.

"The body of a fairly well-developed and well-nourished young male. There is no edema, and rigor mortis is present in both upper and lower extremities. The pupils are equal and normal in size. There are marked areas of hemorrhage into the walls of the intestine at irregular scattered intervals throughout its entire length. The mesenteric lymph nodes are slightly enlarged and firm, and on section are of a gray, translucent color. The pericardial and pleural cavities are negative. The myocardium is dark red and firm, and there is no hypertrophy, dilatation or valvular lesion of the heart. Both lungs show the same condition. The pleural surface is dark red in color, but smooth and glistening, and on section the cut surface is dark red also. The consistency is considerably increased, but on pressure a considerable amount of blood-stained fluid and air escapes. The cut surface of the upper lobe of the left lung shows numerous elevated patches scattered throughout, which, however, on account of the poor light available, cannot be certainly diagnosed, but which suggest the hemorrhage of bronchopneumonia. The bronchial lymph glands are apparently normal. The spleen is slightly increased in size and its capsule is normal, but on section the Malpighian bodies are found to be of increased prominence and slightly decreased consistency. The gastrointestinal tract shows numerous areas of hemorrhage into the mucous membrane, of varying size and shape. The most marked area is in the ascending colon next the cecum, covering fully 10 cm., and encircling the entire gut wall. Other areas are not large and there is no evidence of ulceration. The stomach and pancreas are negative; the liver shows marked congestion; on section the cut margin rolls out, and the consistence is slightly decreased. The adrenals are negative. The kidneys are normal in size; on section the cut margin rolls out, the surface markings are somewhat indistinct, but the consistency is normal. The genitourinary tract is normal. The brain shows marked congestion of the pia arachnoid vessels over both the cortex and the base. Examination of the base of the brain shows a distinct puriform exudate into the meninges over the anterior and posterior perforated spaces, and, to a less degree, in the meninges of the immediate neighborhood. In this region, as well as elsewhere, numerous small tubercles are found widely scattered, but chiefly along the course of the blood vessels and involving their walls. The miliary tubercles are most numerous in the meninges between the cerebellum and temporal lobes, and over the median surface of each hemisphere where there is more or less adhesion to the superior longitudinal fissure. Section shows dilatation of the lateral ventricles, which are filled with turbid fluid. The ependyma is slightly congested, both in the lateral and fourth ventricles, and contains numerous very small tubercles.

"The histological examination showed marked congestion of the lungs, with hemorrhages into the alveoli and numerous miliary and conglomerate tubercles composed of small round cells, epithelioid cells and giant cells, the centers of some of which showed caseation and early organization. The bronchi also contained considerable blood. The spleen showed slight congestion of the blood vessels, and also miliary and conglomerate tubercles. The mesenteric lymph nodes showed slight congestion of the blood vessels and considerable proliferation of the endothelial cells of the lymph sinuses. Miliary and conglomerate tubercles were also present in the liver, and showed only slight caseation.. The blood vessels showed moderate congestion. The liver cells were negative. The kidneys showed marked parenchymatous degeneration of the epithelial cells, marked congestion of blood vessels, but no casts. At one point in the cortex a definite miliary tubercle was found. The brain showed marked infiltration with lymphoid cells, and proliferation of epithelioid cells throughout the meninges, especially well marked about the blood vessels. Only a few giant cells were present. There was considerable diffuse caseation, and some of the blood vessels showed marked proliferation of endothelium. Other sections revealed many miliary tubercles lying in the pia arachnoid coat, most of which consisted merely of round cells and epithelial cells with slight caseation. The histological diagnosis is as follows: Acute disseminated tuberculosis of the lung, spleen, liver and kidney, with early, acute tuberculous meningitis.

"Cover slips from the meninges stained for tubercle bacilli showed them present in large numbers. Cover slips and cultures from the meninges of the brain, heart's blood, spleen and lymph nodes gave negative results."

It appears from an examination of the literature of this subject that tubercular meningitis, complicated by a secondary infection, is either very rare or rarely recognized. Heiman found the tubercle bacillus and the diplococcus of pneumonia in the exudate of a case of meningitis. Lenhartz and Heubner found the tubercle bacillus and the meningococcus associated in three cases of cerebrospinal meningitis. Holdheim found the meningococcus in the spinal fluid, and at the autopsy the case was shown to be one of tuberculous meningitis. This appears to exhaust the literature on the subject. It may be mentioned that Stadelman is sceptical regarding the occurrence of the meningococcus and the tubercle bacillus together. Of course, it would be of interest if a difference could be recognized in the clinical pictures of cases of tuberculous meningitis with mixed infection and those without it. In the brief published notes of the cases that we have collected the clinical history is either given not at all, or so incompletely that no conclusions can be drawn. In our own case the signs of spinal involvement were very slight, in this agreeing with the usual picture of tuberculous meningitis. Retraction of the head was not distinct; there was no rigidity of the spine, and the patient complained only moderately of pain in the limbs. Indeed, the predominant symptoms were those of severe septic infection, involving the cerebral hemispheres, and, therefore, the existence of malignant endocarditis was suspected when the case was first seen. When the symptoms of cerebral meningitis had become fully developed it was not understood why there was no leucocytosis. Kernig's sign was present, and our experience leads us to agree with Dieulafoy and Packard, that it is rare in tuberculous meningitis, but not so uncommon as to make its presence of especial significance.

In the study of this case there were two unfortunate omissions, both due to circumstances beyond our control. No inoculations were made with the first specimen of spinal fluid obtained, as animals, unfortunately, were not then available. No cultures were made from the meningeal exudate at the time of the autopsy. Dr. Hendrickson performed this autopsy under most unfavorable conditions in one of the suburbs of Philadelphia, and it was impossible to make cultures there, or to transfer the material in an aseptic condition to the laboratory. There appears, however, to be no reasonable doubt of the existence of both forms of infection. The finding of the tubercle bacillus in the smears and the histological picture proves conclusively that tuberculosis was present; and the fact that the same micro-organism was obtained in the spinal fluid on two occasions proves, I think, that it could not have been due to accidental contamination, especially as the cultures were made with great care and under very favorable conditions.

LITERATURE.

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